REMARKS

Claims 1-22 have been previously cancelled without prejudice. Claims 23-34 have been previously added to replace claims 11-22. By this amendment, Applicants have added the molecular weight of laminarin to claim 1 which is supported in the original specification (e.g., page 4, lines 23-24 of the description). Applicants submit that upon entrance of the present amendments, the present application will overcome the prior rejections and will be placed in condition for allowance for the reasons as set forth below.

Claim objections

Rejection under 35 USC§103

In the Official Action, the sole rejection of Claims 23-34 was under 35 U.S.C. 103(a) as being unpatentable over the Tsuzuki et al. reference in view other Fan et al. reference. This rejection is respectfully traversed for the reasons set forth below.

The arguments submitted in our response to the last Office Action are herein repeated.

Tsuzuki et al. examined the relationship between the conformation of Sonifilan (SPG) and hematopoietic responses in cyclophosphamide-induced leukopenic mice. Tsuzuki et al. disclose that the mice administered cyclophosphamide and SPG or SPG-OH expressed and produced higher levels of IL-6, NK1.1, SCF and M-CSF, than the mice administered only cyclophosphamide.

Even if these results may suggest a potent activity of SPG and SPG-OH on hematopoieisis, further *in vivo* results would have been necessary to convince one skilled in the art that SPG and SPG-OH could stimulate the regeneration of cells in the bone marrow and the peripheral blood.

As indicated in Professor Vaclav Vetvicka's declaration under Rule 132 (copy already furnished), Sonifilan is a polysaccharide produced by the fungus *Schizophyllan commune,* whereas laminarin is a polysaccharide produced by the brown algae. Furthermore, these two glucans have a different molecular weight and conformation.

These two glucans can thus not be directly compared. The results obtained with Sonifilan cannot be obviously extrapolated to Laminarin, and *vice versa.*

Fan et al. disclose a polysaccharide extracted from *Luminaria japonica,* called by the authors "laminarin". According to Fan et al., this polysaccharide contains 60.4% of sugars, has a molecular weight of 40,000, and an acute toxicity LD5O of 980 mg/kg.

The laminarin of the claimed invention is dramatically different.

First, the laminarin of the claimed invention is preferably extracted from *Laminaria digitata* or *Laminaria saccharina* (see page 6, lines 13-30), whereas the polysaccharide of Fan et al. is extracted from *Luminaria japonica.*

Second, the laminarin of the claimed invention has a molecular weight from about 2,500 to about 6,000 (see e.g., page 4, lines 23-24), which is extremely far from 40,000. In this respect the average degree of polymerization of the laminarin of the claimed invention is close to 25 (see e.g., page 4, line 30). Accordingly the polymerization degree of the "laminarin" of Fan et al. must be much higher to attain a molecular weight of 40,000.

Third, the laminarin of the claimed invention is only composed of glucopyranose units (see e.g., page 4, lines 25-29) and the terminal unit of the main chain consists of glucose or mannitol (see e.g., page 5, lines 1-3). To the contrary, the "laminarin" of Fan et al. only contains 60.4% of sugars, the remaining 39.6% being undefined, but may be, as far as the Fan et al. reference is understandable, proteins and nucleic acids.

Last but not least, the laminarin of the claimed invention is safe and presents an acute toxicity LD5O in the rat greater than 2,000mg/kg (see e.g., page 15, lines 3-5). Conversely, the "laminarin" of Fan et al. presents an acute toxicity LD5O in mice of 980mg/kg, which constitutes a huge difference of more than two fold.

Consequently, in view of the huge differences disclosed above, it is clear that the polysaccharide of Fan et al. and the laminarin of the claimed invention are totally different.

As a result, even if the polysaccharide of Fan et al. may have an antagonistic action on leucopenia, one having ordinary skill in this art would **not** have concluded anything concerning the activity of the laminarin of the claimed invention. Indeed, in the

field of pharmacology, a small difference in a molecule may change its biological activity. In this case, the differences are numerous and huge, and thus the biological activity of laminarin of the invention is entirely unpredictable in view of Fan et al.

Consequently, the data disclosed in Fan et al. can in no way suggest or make it obvious that laminarin can have an effect on the hematopoiesis of animals/humans subjected to an hematotoxic challenge;

Hence, the skilled artisan, reading Fan et al., cannot conclude anything regarding the laminarin and activation of hematopoiesis.

The present invention is thus unobvious in view of Tsuzuki et al. and Fan et al., taken alone or in combination.

From the foregoing remarks, Applicants submit that the instant invention as defined in the claims is unobvious over the cited prior art. Thus, the Examiner's rejection under 35 U.S.C. §103 on the basis of the cited references is respectfully traversed and should be withdrawn.

In view of the above amendments and remarks, it is clear that the present amendments will place this application and all of its claims in condition for allowance, and that the amendment should thus be entered. Entrance of the amendment and the issuance of a Notice of Allowance is therefore respectfully solicited. Should the Examiner believe that a discussion with the undersigned counsel would expedite prosecution of the application, a telephone call to (703) 739-4900 would be welcomed.

Respectfully submitted,

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